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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/917,376	DING ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2003 and 19 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-12,14,15,28,30-36 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-12, 14, 15, 28, 30-36, and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Amendment of June 23, 2003, in response to the Final Rejection of March 11, 2003, and Applicant's response, of March 19, 2004, to the Election/Restriction requirement of January 16, 2004 are acknowledged. Claims 1, 2, 4-12, 14, 15, 28, 30-36, and 43 are pending. It is acknowledged that applicants have amended Claims 1, 9, and 10.

Applicant's election with traverse of Invention I, Claims 1, 2, 4-6, 10, 11, 14, 15, 28, 30-36, and 43, in part, and 7, 9, and 12, as well as the species leucince zipper, in their response of March 19, 2004 is acknowledged. The traversal is on the ground(s) that no undue burden would be imposed by examination of multiple groups, such as I and II, since a search for Group I would encompass a search for Group II. These arguments have been considered and all claims, Claims 1, 2, 4-12, 14, 15, 28, 30-36, and 43, are hereby reconsidered.

Claims-Objections

The claim set is objected to for failing to indicate that Claims 16-27 and 37-42 are canceled.

Claims 10 and 11 are objected to for poor grammar. Claim 10 would be more clearly stated as: "The composition of claim 1, wherein the catalytic domain of GH74_Ace has at least 90% sequence identity with SEQ ID NO: 3". Claim 11 would be more clearly stated as: "The composition of claim 1, wherein the catalytic domain of GH74_Ace has at least 80% sequence identity with SEQ ID NO: 3".

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-11, 14, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in reciting "... a substantially purified AviIII peptide...", as said recitation does not define an activity for the claimed peptide. The specification defines AviIII polypeptides activity as a substrate binding activity or a cellulase activity (pg 18, lines 6-7). Thus, it is not clear what activity, if any, is being recited in Claim 1. Claims 2, 4-11, 14, 15 are rejected as being indefinite for the same reasons.

Claim 7 is indefinite in reciting "...defined as a polypeptide sequence of SEQ ID NO: 4". It is not clear whether said claim is meant to recite any fragment of SEQ ID NO: 4 or the complete sequence of SEQ ID NO: 4.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

In this regard, the application disclosure and claims are compared per the factors indicating in the decision re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4)

the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 1-2, 4-11, 14, 15, 28, and 30-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 1, does not reasonably provide enablement for any polypeptide having a GH74 domain homologous to SEQ ID NO: 3 and a CHB domain or a polypeptide comprising at least one of SEQ ID NO: 1 and 3-5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 2, 4, 5, 14, and 15 are so broad as to encompass any polypeptide comprising a GH74 catalytic domain that is at least 70% identical to SEQ ID NO: 3 and a CBD III domain. Claim 6 is so broad as to encompass any polypeptide comprising SEQ ID NO: 3 and a CBD III domain. Claim 7 is so broad as to encompass any polypeptide comprising a GH74 catalytic domain that is at least 70% identical to SEQ ID NO: 3 and the CBD III domain set forth by SEQ ID NO: 4. Claim 8 is so broad as to encompass any polypeptide comprising a GH74 catalytic domain that is at least 70% identical to SEQ ID NO: 3 and the CBD III domain set forth by SEQ ID NO: 5. Claim 9 is so broad as to encompass any polypeptide comprising the GH74 catalytic domain set forth by SEQ ID NO: 3 and the CBD III domain set forth by SEQ ID NO: 4. Claims 10 and 11 are is so broad as to encompass any polypeptide comprising a GH74 catalytic domain that is at least 90% and 80% identical, respectively, to SEQ ID NO: 3 and a CBD III domain.

Claims 28 and 30-43 are so broad as to encompass any polypeptide comprising at least one of SEQ ID NO: 1 and 3-5. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the polypeptide of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the Claims 1-2, 4-11, 14, 15, 28, and 30-43 which, encompasses all polypeptides comprising at least one of SEQ ID NO: 1 and 3-5, or variants thereof, having no recited activity. The specification does not support the broad scope of Claims 1-2, 4-11, 14, 15, 28, and 30-43 because the specification does not establish: (A) the activity of all polypeptides comprising at least one of SEQ ID NO: 1 and 3-5 and variants

thereof; (B) regions of the protein structure, other than the residues designated with an asterisk in Claim 1, which may be modified without effecting the desired activity; (C) the general tolerance of the desired activity to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues, other than the residues designated with an asterisk in Claim 1, with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptides comprising at least one of SEQ ID NO: 1 and 3-5, or variants thereof, having no recited activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicant's arguments: In support of Applicant's request that rejection of Claims 1-2, 4-11, 14, 15, 28, and 30-43 under 35 U.S.C. 112, first paragraph, for lack of enablement be withdrawn, they provide the following arguments. "It is alleged that these claims, including at least claims 1, 14 and 15, are not supported by a specification that teaches any thermostable AviIII peptide having a GH74 domain. As to claims 1, 14, and 15, the Examiner asserts that knowledge and guidance are required to determine which amino acids, if any, are tolerant of

modification, as well as those which are conserved and presumably not subject to modification. This issue has been resolved by deleting the word "thermostable" from claims 1, 2, 4, 5, 12, 13 and 14 in each instance, and by amending claim 1 to recite the positional identity of sequences in comparison to AviIII_Aac shown in Table 3 on page 34 of the application as filed."

The amendments to claim 1 are made to show that Applicants did disclose which amino acids are tolerant of modification. Applicants previously traversed the rejection because such information is provided, for example, on pages 32-33 of the Specification in Example 2 and Table 3, which provide those skilled in the art with sufficient information to make these determinations by observing the conserved sequences among the GH74 family. Now that comparison is specifically claimed in claim 1. The remaining objections as to claims 2-5, 6-9, 28-36, and 43 are postulated for identical reasons, and Applicants similarly traverse these objections. The recitation in claim 1 of 70% sequence identity is made in context of preserving these conserved sequences."

Reply: These arguments are not found to be persuasive for the following reasons. Claims 1-2, 4-11, 14, 15, 28, and 30-43 were never rejected under 35 U.S.C. 112, first paragraph, because the specification did not support the recitation of "thermostable" in the claims. Therefore, amendment to remove the recitation of "thermostable" is not relevant to the rejection. It is acknowledged that Claim 1 has been amended to recite the positional identity of sequences, in comparison to AviIII_Aac, that are to be conserved. However as described above, such limitations do not enable a person of ordinary skill in the art to make and use all of the AviIII peptides recited in the rejected claims. The specification fails to provide sufficient guidance to enable the skilled artisan to determine, without undue experimentation, which of the peptides

having a catalytic domain having 70% identity with SEQ ID NO: 3, wherein the catalytic domain comprises each of the conserved residues indicated by an asterisk in Claim 1, have the desired enzymatic or biological function desired. For these reasons and those discussed in detail above, rejection of Claims 1-2, 4-11, 14, 15, 28, and 30-43 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained.

Written Description

Claims 1-2, 4-11, 14, 15, 28, and 30-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of protein molecules comprising at least one of SEQ ID NO: 1 and 3-5, or variants thereof.

The specification does not contain any disclosure of the function of all said protein molecules. The genus of polypeptides that comprise these above protein molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated polypeptides are encompassed within the scope of these claims, including partial peptide sequences. The specification discloses the function of only a single species of the claimed genus, the cellulase of SEQ ID NO: 1, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-2, 4-11, 14, and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Recitation in Claim 1 of "...a catalytic domain of a glycosyl hydrolase family 74 (GH74_Ace) enzyme having at least 70% identity to SEQ ID NO: 3..." is not described in the specification and constitutes New Matter. Applicants state in their response of June 23, 2003 that said recitation is supported on page 19, lines 3-4 of the specification. However, said lines state: "The amino acid sequence of AviIII polypeptides of the invention is preferably at least about 60% identical, more preferably at least about 70% identical, or in some embodiments at least about 90% identical, to the AviIII amino acid sequence shown above in Table 1 and SEQ ID NO:1." Thus, said lines do not disclose a polypeptide having a GH74_Ace domain that has 70% identity to SEQ ID NO: 3. Claims 2, 4-11, 14, and 15, as dependent on Claim 1, are rejected for the same reason.

Applicant's arguments: In support of Applicant's request that rejection of Claims 1-2, 4-11, 14, 15, 28, and 30-43 under 35 U.S.C. 112, first paragraph, for insufficient written description be withdrawn, they provide the following arguments. "...the substance of the rejection is that only a single representative species of the claimed genus is disclosed in the written description, yet the genus pertains to any GH74 catalytic domain peptide having a CBDIII domain.

Amended claim 1 overcomes the rejection by specifically reciting which sequences are tolerant to modification. Examples 2 and 3 on pages 33-35 of the specification as filed show a rationale for observing the conserved identities between GH74 Ace and AviIII_Aac, as is now specifically recited in claim 1. Example 3 mentions that fusion proteins and site-directed

mutagenesis may be availed, for example, to provide a variety of sequences in a genus context. Applicants have disclosed and claimed a rationale for making the claimed genus by virtue of the conserved sequences recited in claim 1, and the segmented combinations of claim 28. As such, Applicants have disclosed more than a single working embodiment.

Whether such changes may be made according to the 70% homology of claim 1 while preserving thermostability is now a moot issue, since thermostability has now been deleted from the claims in each instance. Even so, thermostability is an inherent characteristic of claims 6, 9, 12, and 28, which call out identity with respect to sequences that are known to be thermostable.

Claims 28-36 and 43 are further rejected because the claims are directed to a genus of sequence homology, e.g., 70% identity with SEQ ID No. 1, but none of the homologous sequences are specifically disclosed. Claim 28 has been amended to delete reference to this homology and, consequently, overcomes the rejection. Claim 43 depends from claim 1 where the objection is overcome by the different recitation, as discussed above."

Reply: These arguments are not found to be persuasive for the following reasons. As stated by Applicants themselves, "GH74 family enzymes are not highly conserved in the catalytic domain. The attached Rule 1.32 Declaration from Dr. Himmel documents computer research showing that, among 12 reported GFH74 family sequences, the highest rate of homology is about 50%." (pg 13, parg 4, lines 1-4; Response of June 23, 2003). Thus, recitation of a peptide containing any GH74 catalytic domain does not constitute sufficient written description. It is acknowledged that Claim 1 has been amended to specifically recite which sequences are tolerant to modification. However, as described above, the rejected Claims do not recite the activity or biological function of the recited sequences and, therefore, the sequences are

not adequately described. The described use of fusion proteins and site-directed mutagenesis in the specification fails to over come the lack of written functional description for the recited peptides. The issue of "thermostability" is, again, not relevant. It is acknowledged that Claims 28-36 and 43 have been amended to delete reference to "70% identity with SEQ ID NO: 1". However, as discussed above for the rejection of Claims 28 and 30-43 under 35 U.S.C. 112, first paragraph, for insufficient written description, the neither the specification nor the amended claims describe the function of the recited sequences.

For these reasons, rejection of Claims 1-2, 4-11, 14, 15, 28, and 30-43 under 35 U.S.C. 112, first paragraph, for insufficient written description is maintained.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 1, 2, 4-12, 14, 15, and 28 under 35 U.S.C. 103(a) as being unpatentable over Mohagheghi et al, 1986 in view of Berghem et al, 1976 and Katz et al, 1968, for the reasons set forth in the First Action on the Merits and the Final Rejection, is maintianed. Rejoined Claim 43, which recites a composition comprising the polypeptide of Claim 28, is rejected for the same reasons.

Applicant's arguments: In support of Applicant's request that rejection of Claims 1, 2, 4-12, 14, 15, and 28 were previously rejected under 35 U.S.C. 103(a) be withdrawn, they provide the following arguments. (i) Although Bronnemeir et al, 1991 and Tan et al., 1986 are not cited as references in formulating the 103 rejection, the teachings of Bronnemeir et al and Tan et al, are applied for the rejection. (ii) "It is not sufficient that the Examiner can propose a modification of Berghem et al., via Bronnenmeir et al and Tan et al., to show other methods that have been used to isolate exoglucanases and endoglucanases as a class of materials. The examiner must specifically show isolation of a GH74 family exoglucanse having the sequences that are specifically claimed." It could not have been predicted that those of skill would successfully locate a GH74 family exoglucase from *A. Celluloyticus*, much less the sequence that is recited in claim 12. (iii) Berghem et al teach the isolation of an endoglucanase, not the exoglucanase of the instant application. Thus, the combination does not teach or suggest all of the claim limitations because, the combination would merely result in the isolation of an endoglucase from *A. cellulolyticus*. (iv) "Besides, where endoglucanases and exoglucanases both have affinity for Avicel, this would not serve to isolate either type of enzyme exclusive of the other." (v) "GH74 family enzymes are not highly conserved in the catalytic domain. The attached Rule 132 Declaration from Dr. Himmel documents computer research showing that, among 12 reported GFH74 family sequences, the highest rate of homology is about 50%. Claim 1 distinguishes the art by reciting at least 70% sequence identity."

Reply: These arguments are not found to be persuasive for the following reasons. (i) The teachings of Bronnenmeir et al and Tan et al, were not necessary for the original rejection of Claims 1, 2, 4-12, 14, 15, and 28 under 35 U.S.C. 103(a), but were merely used to rebut

Applicant's arguments in the response of December 16, 2002. (ii) It is not necessary for the prior art to teach the specific sequence of the isolated glucanase or that the isolated glucanase would have a GH74 domain, as said sequence and domain are inherent to the isolated protein. It is merely necessary for the prior art to teach a means to isolate the recited protein and motivation to do so. (iii) As evidenced by Bronnenmeir et al and Tan et al, the method taught by Berghem et al would isolate an exoglycanase. This point is discussed further in the Final Rejection. (iv) It is acknowledged that the method of Berghem et al would simultaneously isolate both endoglucanases and exoglucanases from *A. cellulolyticus*. However, Claims 1, 2, 4-12, 14, and 15 recite "A composition comprising a substantially purified AviIII peptide...". The specification defines purified as "a target protein that is free from at least 5-10% of contaminating proteins" (pg 12, lines 12-13). Thus, Claims 1, 2, 4-12, 14, and 15 encompass compositions comprising both endoglucanases and exoglucanases. Claim 28 recites "An isolated polypeptide...". Since, the specification defines isolated as "...a polypeptide that has been separated from at least one contaminant (polynucleotide or polypeptide) with which it is normally associated", Claim 28 encompasses compositions comprising both endoglucanases and exoglucanases. (v) As described in (ii), the sequence is inherent to the isolated protein.

For these reasons, the rejection of Claims 1, 2, 4-12, 14, 15, and 28 under 35 U.S.C. 103(a) as being unpatentable over Mohagheghi et al, 1986 in view of Berghem et al, 1976 and Katz et al, 1968 is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan Lee Swope, Ph.D.